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DRAFTSMAN

MAQTQGTRRKVCYYYDGDVGNYYYGQGHPMKPHRIRMTHNLLLN

YGLYRKMEIYRPHKANAEEMTKYHSDDYIKFLRSIRPDNMSEYSKQMQRFNVGEDCPV **FDGLFEFCQLSTGGSVASAVKLNKQQTDIAVNWAGGLHHAKKSEASGFCYVNDIVLAI LELLKYHQRVLYIDIDIHHGDGVEEAFYTTDRVMTVSFHKYGEYFPGTGDLRDIGAGK** TIKGHAKCVEFVKSFNLPMLMLGGGGYTIRNVARCWTYETAVALDTEIPNELPYNDYF **EYFGPDFKLHISPSNMTNQNTNEYLEKIKQRLFENLRMLPHAPGVQMQAIPEDAIPEE** SGDEDEDDPDKRISICSSDKRIACEEEFSDSEEEGEGGRKNSSNFKKAKRVKTEDEKE GKYYAVYPLRDGIDDESYEAIFKPVMSKVMEMFQPSAVVLQCGSDSLSGDRLGCFNL KDPEEKKEVTEEEKTKEEKPEAKGVKEEVKLA (SEQ ID NO:1)

FIG. 1A

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(SEQ ID NO:2) tgagaacaca atggcgcaga aattactatt ttgctgctca gctgaggaga ccagataaca ccagtattcg gctgtgaaac catgcaaaga ctggaactgc gacggcgtgg tatggagagt tattatgctg ttcaagccgg tgtggctcag ggtggttaca gatacggaga ttcaagctcc aagatcaaac acgcaggcga cctgacaagc tccgattctg cacgccaagt aagagagtca gaagaggaga ttggcctgaa บ teggtcatec ggcgagcaag gactcataat ctccatccgt tgtggcaagt tcaccatggt caaagacaag tgaggccatt ggtcttacag tatcaaagga ggaagagttc aggaatcacc tttctttccc ggatgttgga caaagccaat tgaggactgt gggcctgcac cttggccatc cttcataag gctgggaggc tgtggccctg tggaccagat gtacctggag tggggtccaa cgaagacgac caaaaagcc ggaggccaag tgtctcccac cacgcgggga ctagtgcggt atgagacagc gggtcaagga actacgacgg gaatccgcat atcgccctca ctggtggttc attgggctgg acattgatat tgactgtgtc acgagtccta acacgaatga gcgatgagga ttgcctgtga aggagagaa gtccctcacg aattcttgcg tcaacgttgg atgatatcgt ccggggctgg tcaatctatc ctatgctgat ttgaatactt cgcacgcacc cttccaactt ctggtgctgc cggggtagac tttaacctgc ttcctgctga gtctgttact aagcctcacc atcgccgtga tgttacgtca ctgtacattg gaccgggtca ctacgggata gggattgatg atgttccagc agaatgctgc gaggagagtg aaagacccag gaagccaaag atggaaatct gactacatta atgcagagat cagttgtcta ttaggttgct tgctggacat aatgactact actaaccaga gacaaacgaa cgcaagaact tctctgcccg ctctgtcact ccggaggaaa ccacccaatg ctaccgaaaa gcagacggac atctggcttc ccagagggtg ctacaccacg aactggggac gctccgagac agtaatggag tggggatcgg tgtcaagagc cgttgcccgg gcttccatac ttccaatatg agagggggc tgaaaaagag ggagaagcca cagctctggc ccacagcgat cagcaagcag tgagttctgt tgagaacctt cgccatccct ctgctcctct atgtctgggg gcctgagcgr aaacagagga aaaccaagga cgcagggcac atggacaagg tgaccaagta tgtcggagta agtccgaggc taaagtatca acttcccagg ttaactaccc tcatgtccaa actccctatc ccattcgtaa tccctaatga acatcagtcc ttcctgagga tggacctctc actatggtct atggcctgtt ttaataagca aagaggcctt gtgtggaatt agcgactgtt gcatctcgat aagaggaggg 61 181 601 1081 1141 1201 1261 1321 1381 1441 121 241 301 361 481 541 661 721 841 901 961 1021 1501 781

# FIG. 1B

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NYGLYRKMEIYRPHKATAEEMTKYHSDEYIKFLRSIRPDNMSEYSKQMHIPFNVGEDCP LTVKGHAKCVEVVKTFNLPLLMLGGGGYTILRNVARCWTYETAVALDCEIPNELPYNDY **AFDGLFEFCQLSTGGSVAGAVKLNRQQTDMAVNWAGGLHHAKKYEASGFCYVNDIVLA** KGKYYAVNFPMCDGIDDESYGQIFKPIISKVMEMYQPSAVVLQCGADSLSGDRLGCFN FEYFGPDFKLHISPSNMTNQNTPEYMEKIKQRLFENLRMLPHAPGVQMQAIPEDAVHE ILELLKYHQRVLYIDIDIHHRGDGVEEAFYTTDRVMTVSFYGEYFPGTGDLRDIGAG DSGDEDGEDPDKRISIRASDKRIACDEEFSDSEDEGEGGRNVADHKKGAKARIEED KKETEDKKTDVKEEDKSKDNSGEKTDTKGTKSEQLSNP (SEQ ID NO:3) MAYSQGGGKKKCKVCYYYDGDIGNYYYGQGHPMKPHRIRMTHNLLL

FIG. 2A

|            |         |          |          |          |            |          |          |          |          |          |            |          |          |          |            |          |          |          |          |          |            |            |          |          |          |           |          |          |            |          |          |           | 1        |
|------------|---------|----------|----------|----------|------------|----------|----------|----------|----------|----------|------------|----------|----------|----------|------------|----------|----------|----------|----------|----------|------------|------------|----------|----------|----------|-----------|----------|----------|------------|----------|----------|-----------|----------|
| C.         | agccctt | aggagccc | aaaaag   | cccatgaa | agaaaaat   | agtgatga | aagcagat | ttttgtca | actgatat | ggatcctg | gagtett    | acaacaga | ggagactt | tgtgatgg | atggagat   | gatagact | aaaacttt | gctcga   | ccatataa | aacatgac | aatttgcg   |            | gcatcaga | gaggt    | gataaga  | aacagtgg  | atctgaca | tctttt   | tcaaatgg   | aagc     | agttatt  | aaaaaaa   |          |
| tacadaaaa  | cgtttcc | cagcagga | ggcggca  | acagggtc | tggcttac   | aaaatatc | tgagtata | ctctttg  | ccgacaac | gaagcat  | gtatcatc   | agctttt  | tcctggca | ttttccaa | aaagg      | attatctg | agaagttg | cgtaatg  | caacgagt | agtcctt  | ttgtttg    | gaagatg    | ctattc   | tgaaggag | aattgaag | atccaagg  | caaccct  | aggaaaat | atttat     | attttcta | aattgatg | gaa       |          |
| gadcc      | atcgccc | cagcagc  | acagtca  | attat    | ctgttaaatt | aagaaatg | ataacatg | cgttt    | tgaagtta | ctaagaaa | attacta    | gtgtcgaa | gggaatac | atgctgtc | agcctat    | gtgcagac | ctaaatgt | ctacaca  | gtgagat  | aactgcat | taaaacag   | caagctattc | aca      | attctgag | agaaagc  | aagaagat  | ţ        | aaat     | atgga      | ttattgtg | tagtat   | ccttt     |          |
| taccagataa | cgcggga | ggcag    | ccatggc  | attgga   | cataactt   | gccactg  | ga       | gattgtcc | gctggagc | ttacatc  | ccatcct    | catggtga | cataaa   | ggcaaata | gcagatattt | ttacagtg | aaaggtca | b        | gcccttga | ccagactt | acggaaaa   | cag        | gaagatcc | gaattct  | ag       | gacgtt    | accaaatc | attaaaaa | tatactactt | tgggcaag | tttatgt  | aagaagta  |          |
| cggcacc    | ctt     | Ū        | gccgggg  | aggt     | catg       | CCa      | a<br>C   | tggag    | ttca     | tggag    | atattgtgct | tattc    | atca     | tggaa    | atat       | tgtgg    | aacag    | gat      | tgcag    | tttt     | agaat      | acctg      | agat     | tgatg    | tcat     | acaaaaaac | caaag    | gaaa     | gcttcatt   | tttgttt  | acc      | tgatctat  | D NO:4   |
| ccgagct    | tcccacc | tctcccgg | cggcg    | gctactac | ctcataga   | aaatatat | atatcaaa | atatattt | tctcaact | ctgttaat | Ţ          | atatcgat | gtgtaatg | gggatatt | tagacgat   | atcaacct | gttgtttc | acttacca | ggacatat | attacttt | accagaac   | tgttacct   | cagtgga  | agcggata | gaaatgtg | aacagag   | aaaaaca  | ctcaccaa | aagacttc   | ctttttcg | aatttctt | gtcaaaaaa | aaag (SE |
| <b>H</b>   | 61      | 2        | $\infty$ | 4        | 0          | 9        | N        | Φ        | 4        | 0        | 9          | N        | $\infty$ | 4        | 0          | 96       | 07       | 80       | 14       | 20       | <b>5</b> 6 | 32         | 3        | 14       | 20       | 56        | 62       | 9        | 74         | 80       | 1861     | 92        | 9        |

Jan II Ibrig Jr 10 Jan Ibrig II I

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# **MAKTVAYFYDPDVGNFHYGAGHPMKPHRLALTHSLVLHYGLYKK**

**CECVEYVKSFNIPPLLVLGGGGYTVRNVARCWTYETSLLVEEAISEELPYSEYFEYFAP** MIVFKPYQASQHDMCRFHSEDYIDFLQRVSPTNMQGFTKSLNAPNVGDDCPVFPGLFE **HPRVLYIDIDIHHGDGVQEAFYLTDRVMTVSFHKYGNYFFPGTGDMYEVGAESGRYYC** LNVPLRDGIDDQSYKHLFQPVINQVVDFYQPTCIVLQCGADSLGCDRLGCFNLSIRGH FCSRYTGASLQGATQLNNKICDIANWAGGLHHAKKFEASGFCYVNDIVIGILELLLKY **DFTLHPDVSTRIENQSRQYLDQIRQTIFENLKMLNHAPSVQIHDVPADLLTYDRTDE** ADAEERGPEENYSRPEAPNEFYDGDHDNDKESDVEI (SEQ ID NO:5)

# FIG. 3A

APP. 1211

**MLAMKHQQELLEHQRKLERHRQEQELEKQHREQKLQQLKNKEKG** 

KESAVASTEVKMKLQEFVLNKKKALAHPNLNHCISSCPRYWYGKTQHSSLDQSSPPQS GVSTSYNHPVLGMYDAKDDFPLRKTASEPNLKLRSRLKQKVAERRSSPLLRRKDGPVV

TALKKRPLDVTDSACSSAPGSGPSSPNNSSGSVSAENGIAPAVPSIPAETSLAHRLVA **REGSAAPLPLYTSPSLPNITLGLPATGPSAGTAGQQDTERLTLPALQQRLSLFPGTHL** 

**TPYLSTSPLERDGGAAHSPLLQHMVLLEQPPAQAPLVTGLGALPLHAQSLVGADRVSP** 

SIHKLRQHRPLGRTQSAPLPQNAQALQHLVIQQQHQQFLEKHKQQFQQQQLQMNKIIP

KPSEPARQPESHPEETEEELREHQALLDEPYLDRLPGQKEAHAQAGVQVKQEPIESDE

EEAEPPREVEPGQRQPSEQELLFRQQALLLEQQRIHQLRNYQASMEAAGIPVSFGGHR

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PLSRAQSSPASATFPVSVQEPPTKPRFTTGLVYDTLMLKHQCTCGSSSSHPEHAGRIQ

SIWSRLQETGLRGKCECIRGRKATLEELQTVHSEAHTLLYGTNPLNRQKLDSKKLLGS

LASVFVRLPCGGVGVDSDTIWNEVHSAGAARLAVGCVVELVFKVATGELKNGFAVVRP

PGHHAEESTPMGFCYFNSVAVAAKLLQQRLSVSKILIVDWDVHHGNGTQQAFYSDPSV

LYMSLHRYDDGNFFPGSGAPDEVGTGPGVGFNVNMAFTGGLDPPMGDAEYLAAFRTVV

**MPIASEFAPDVVLASSGFDAVEGHPTPLGGYNLSARCFGYLTKQLMGLAGGRIVLALE** 

QRTTSTAGRSLIEAQTCENEEAETVTAMASLSVGVKPAEKRPDEEPMEEEPPL (SEQ ID NO:7) GGHDLTAICDASEACVSALLGNELDPLPEKVLQQRPNANAVRSMEKVMEIHSKYWRCL

FIG. 4A

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| FIG. 4B-1 | FIG. 4B-2 | FIG. 4B-3 | FIG. 4B-4 | FIG. 4B-5 |
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|--------------------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| cccgagcccg<br>acctddacc  | SESSESSES  | ctagagccgg | cattgtccgc | tggacgccgc | decdededec | acadadacda | agcggcgccg | agcggacgcc | cggcgcttga | agtttggagc | aaaggagtgg | agaccagcca | tgtggccacg | ggaccaccag | ggagctcctg |
| gccgcccgag<br>acadcctccc | agcccgagcc | cggagcaggg | gcccgcgggc | ccgcggcagg | gccagcgctg | gacctttcca | cacggcaggc | tgcagaagcc | cggcgaggct | tgttggcggg | cgaatcactt | tttctggccg | gcacggtgga | acccgcgcct | agctgcagca |
| cgtccccgcc               | tagaagaaag | cgcggagcgc | ccggcccggc | gccttggagc | ggaggcgggg | gcccttctg  | cgggggtggg | caggttcatc | gagaccttgc | tacttgtatg | tgagccattt | ccagatggac | cacatgccca | gegacatag  | cgggagcagc |
| cgcggagcac               | gtcccggctg | ggagatgcgg | aagcgcagcc | cagcctgcag | cgcggccgtg | dddccdcccd | 886888868  | gccccccgag | cctggctcat | accgtcccgg | gtggaaattt | ccaaagccat | ccgcgtgaac | ccccccggca | gccggccctg |
| <u> </u>                 | gtg        | cgcaggctga | ccgccgcggt | gagaaagag  | GCGCCCGCG  | ccggtcccca | cgcccgccgg | cggggcccgc | ttgtgggtta | cccagccctc | tatcgtttcc | caatgagctc | tgaatcccgc | tgcaagtggc | ctgtggcaga |
| ggaggttgtg<br>agcccgcgca | ggcg       | cgggtggcgg | ccdccdccdc | cdcccdcccc | cggtccacac | gtgggacccg | gaggcggctt | tctcccggtg | tctgttcaac | acgtctgtga | tcgttggagc | acattgctag | gtggagctgc | gcgctgcctc | ttctcactgc |
| 61                       | 121        | 181        | 4          | 0          | 9          | N          | S          | 4          | 0          | 9          | 2          | 781        | 4          | 0          | 961        |

# FIG. 4B-

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|----------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| agag     | gcaataacag | gctggagagg | gcagctcaag | gaagttacaa | ctgcacttcc | gagttctcca | cgacgccaaa | CC         | gggcc      | agaaaa     | ac         | tgtggcacga | Ţ          | ct         | บ          | tctgcagcac | gggagtactg | ccacaagctg | cgcccaggct |            |            | ggctctgctg | ggccggcgtg | acgggaggtg | cctcct     | ggccgccggc | acccgcgtct | gacaggcctc | cagccaccc  | cctccggggc |
| cgccga   | agcacatcaa | accagcggaa | agaagctgca | aagtgaagat | atctgaacca | cccttgacca | tgggaatgta | aatc       | aggaaag    | cgcgt      | tcgcgtggag | cgcacagact | ccttgcccaa | agcaggacac | gcacccacct | acagccctct | tcacaggcct | cccctccat  | tgccccagaa | gagaa      | agccaagcga | gtgagcacca | cgcacgcaca |            | gac        | cgtccatgga | cgcagtcctc | cgaggttcac | ggagtagcag | agaagacggg |
| agatcctc | D<br>D     | ctgctggaac | gg         | gccagcacag | gcccaccgga | cagcacagtt | cacccggtcc | gaaccgaatc | ccctgttac  | gtcacagact | Ø          | acgagtttgg | acatcgccat | р          | t          | ggggcagcgc | gcacccctcg | gaccgggtgt | taggaaaaga | cagcagtttc | atcatcccca | gaggagctcc | cagaaggagg | agag       | Ţ          | aactaccagg | ctgtcccggg | cccaccaagc | tgcacctgcg | tecegeetge |
| atccagag | cacga      | ccagcaggag | gagaagc    | gaag       | gaaggcgctg | cgggaaaacg | ctcctataac | aacagcttct | acggagcagc |            | caacaacagc | cccggcggag | tcccctctac | ctctgcgggc | tct        | gcgggacgga | accggcacaa | ggttggtgca | cggaccca   | gcagcagcat | gatgaacaag | ga         | ctgccggg   | b          | cagtgagcag | ccagctgagg | ccacaggcct | gcaggagccc | gaagcaccag | gagcatctgg |
| gaagcagc | ctcccgg    | catgaagc   | gcagga     | agggcaaaga | tcaataaaa  | gctactggta | gagtgtcgac | T)         | ggcc       | taaaaaagcg | cagctcac   | tccccagcat | ccgctccact | ccaccggccc | ccctccagca | cgcccttgga | agcag      | cacagtcctt | cccact     | tca        | gcaact     | ccacccd    | ctggacc    | ggagccc    | gaa        | agcggatcca | taggag     | cgtgtccg   | cgctgatgct | ggaggatcca |
| cgctcaag | acgagcag   | agatgctg   | cgccag     | acaagga    | aatttgtc   | b          | cagago     | gatgacttcc | agcagaa    | tcactgct   | gctccgga   | င်ရွင်င    | ggctcg     | gcctgcct   | accttaca   | gagca      | tggtc      | cccctccacg | ggca       | ctgcagcacc | tcca       | agccggag   | acgageee   | aggtgaag   | đ          | ggagcag    | acagt      | ccac       | tgtatg     | gagcacgccg |
| 1021     | ς<br>Ο     | 14         | 20         | 26         | 32         | 38         | 44         | 20         | 26         | 62         | 89<br>     | 74         | 80         | 86         | 92         | დ<br>დ     | 04         | 10         | 16         | 22         | 28         | 34         | 40         | 46         | 52         | 28         | 64         | 70         | 76         | 82         |

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| Б          |            | .ddc       | tgtg       | caac       | catc       | tagc       | ggct       | cggc       | aatg       | cgtg       | cctg       | ccac       | cgag       | ttac       | ctcc       | ggtc       | ggag       | tgtc       | cgtg       | ctgc       | aggg       | actc       | gagc       | aaaa       | tgta       | ctgt       | gaca     | tgg     | tctg FIG   |
|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|----------|---------|------------|
| しのないなのの    | gttg       | gtg        | tga        | ctactt     | gatect     | cgaccc     | cagcggggct | tttcac     | ggtggt     | cgatgc     | cgggta     | gggagg     | gggaaa     | tgtccgt    | cacaac     | cgagac     | agatga     | cttgtc     | บ          | gccttt     | cctcac     | aagcac     | ದಶ್ವದ      | taatac     | tctctg     | acgg       | gtggggg  | gggag   | tattgc     |
| しいななななないのの | ttg        | cct        | gaaaaatgg  | tgggcttttg | gcgtgagcaa | ctttctacag | tcttcccagg | tcaacacggc | ccttcagaac | catcaggctt | caga       | tggccctcga | ctgccttgct | atgcaaacgc | gcctgcagcg | acgaagaagc | aaaagagacc | ctgctgttct | cacgcctgcg | gccacgggaa | ggcgtggcag | cgcggaagcc | gtggcaacag | aaagatctaa | aactccacag |            | gcacccg  | tgtgagc | acttttttt  |
| ccccccaacc | gtaaggataa | tcggcggggg | acaggggagc | agcacgccca | cagaggttga | acccagcagg | gatgggaact | Ы          | tacttggcgg | gtgctggtgt | aacctctccg | cggattgtcc | gcatgtgttt | caaagaccca | tactggcgct | acttgcgaga | aagcccgccg | ccctcgaa   | tttcccgtgt | gcgtgcaaca | tgcacgcctg | cacacggaca | aaaggagcct | aacaaatatc | tattacccac | ttttttaaag | gcg      | aaacagg | cgagtttgtg |
| tggcacgaac | ctccgtgttc | cgaggtgcac | caaggtggcc | tgcggaggag | gcttctgcag | tggaaacggg | ccgctacgac | gcccggcgtg | 3ct        | cccggatgtg | tgggggctac | ggctggcggc | cgcctcggaa | ggttttacag | ccacagcaag | ggct       | cgtggacgtg | cctgtagcac | gccaagaaac | gggacaccca | gagacgcaca | gacgcgcaga | gccgtggaag | aggcacagaa | gcttaaagtt | ۲          | cggtgtg  | aaactgg | tcggaagatg |
| ניניני     | ct         | atatgg     | b          | tgga       | Б          | cgt        | gtcc       | dddca      | αααα       | cgagtt     | cacccc     | gatgg      | catt       | cccagaaa   | catggaga   | ttctct     | cctcgctgtc | ggagcc     | נג         | gagcacc    | caggtc     | ga         | aad        | gttga      | aaactg     | tcatcttg   | gtgaacca | aaagaaa | tcaaaagcca |
| י<br>ני    | cttcta     | cagtg      | gcgtgg     | ದ್ವದದ್ಧದ   | aadaa      | tggactg    | gtac       | ctgatga    | ggac       | cgatcgcc   | agggccac   | cgaa       | acctgacc   | ttgatcct   | tggagaaa   | cag        | ccgccat    | ccatggaa   | gtctc      | ggctctct   | gcccaggc   | acacggga   | ggcgggtc   | gccgaatt   | aac        | accactcg   | gcccgcct | gggacct | ttga       |
| 94         | 00         | 90         | 12         | 18         | 24         | 30         | 36         | 42         | 3481       | 54         | 09         | 99         | 72         | 78         | 84         | 90         | 96         | 02         | 80         | 14         | 20         | 26         | 32         | 38         | 44         | 50         |          |         | 9          |

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NO:8)

i. 4B-5 H aagaaaag (SEQ gcagggcca gagcgtgttc tctgaagccc tcagtttttc gtctgacaca accggcatga tttctgtaaa ggggatcctg gtgggggac ggggaggcaa tgtgtagcct gtgttctcc ggcactggct cgccactggg cccacgtgcc ggaagaaat ttttgatcag aaatatatat gaagaaaat tattcttaag gtcatattaa tatttatgtg tctctcgagt ccttccacgg ttgagaactg ttacttttag ctgtggttta cacttttttt atggcagagg ttgtagactt cactctttgc caggttatca agagcattac gttccttcat accctgatga ccgcagcgtg ctttggggaa actgcctgtc ccttttatct tttattctga gactttttaa tgtgcgagca taacgaagct ctgctattga cagaacagtg tgcatcatct ggcctggcag tccagggcag aggccttggg tcaaggtgtt tttcgtaatg ttgcttttct attcttcttt atatagatat ggactgtacg ttattgaact ttaaacattt gagtttattg atagccctct cgctgggact gatggaaatt ccctggtggc attcatggca gctcagtggc agtttgcgtc aaaggactac ttcacagtga agtcgtgaac ttcttcattg cattctctgc tggggaggaa cctctgcaaa gtcagggagg tcctttgcaa tttgagggaa tcccgccgtg ggccgtggcc ggccactttg ggaaggacca tgctcattcc agatacaaaa accaataata cttgtgacgg cagctgtgtt aaatgtgctg acagcaagcg atggactttg atatataaat gaggttgcat aactcggcag ttgtttgttt gattaaaagt tccattccc atggagacga ccagcttcac ttgcacgcca agggcgggga ctactcagaa ttgttttgtt cctcactggc ctttccgca cactttaagc aggaaaccat ctctggcatt actttcccct ccgtggctta gatattataa gcgggaccac tttatatccc agcactagca gcattgatac tgacatttgc agaaaataa tacttggaat gactttttat cctcgccgct ctgccccgga ggttctggag gtttgcaagg cacagccacg cctacacctg aacatggact cttgtgacat gaggagctgg gacttgtttg tettetggee ctttactggt ttttattgta ttatctagca cgccgcccgc aaagagtccc ttgcatcgaa tcttaccccg tctcattcaa tcagctcact gacacactcg tggaccttta aagcgagcac tctgacctgc cagcaggcgg tgatttttgc ttttaagttt tatacagatt tcccctctca gaaggagagg tttagggaaa gaattttgtt gctaagattt ctcactttgt atgatgggat gcgtctgcag ccagggctct ttgaaaatct tgttttatgg agattggcaa ccacctgccc ttaattctaa gaaacagtgt tgatttggag ttagctcggc ttttaagcag gtttcatctg tttctttgaa cctcttggcg ctttatattg gaaaaaagt gccaggcgag ggcggactcg gtgatgtatg caattatact acggtcttgg gctagcaggc atctgcctcg tgtgggtcct gggagtcagc cacgcccac cccagcgtc aaagcaagtt aacattcctt tgggcccacg gactttatgt acaaaacctt aaattgtact ttacttctt gaatacattt 6601 6901 7321 7441 7501 7561 7621 7741 921 7981 8101 8161 8221 8281 8401 6661 6841 6961 7021 7081 7141 7381 7681 7801 7861 8041 8341 6721 6781 201 261

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# FIG. 5A

LRQGGTLTGKFMSTSSIPGCLLGVALEGDGSPHGHASLLQHVLL

The state of the s

**LEQARQQSTLIAVPLHGQSPLVTGERVATSMRTVGKLPRHRPLSRTQSSPLPQSPQAL QQLVMQQQHQQFLEKQKQQQLQLGKILTKTGELPRQPTTHPEETEEELTEQQEVLLGE** 

GALTMPREGSTESESTQEDLEEEDEEEDGEEEDCIQVKDEEGESGAEEGPDLEEPGA

GYKKLFSDAQPLQPLQVYQAPLSLATVPHQALGRTQSSPAAPGGMKSPPDQPVKHLFT

TGVVYDTFMLKHQCMCGNTHVHPEHAGRIQSIWSRLQETGLLSKCERIRGRKATLDEI

QTVHSEYIHTLLYGTSPLNRQKLDSKKLLGPISQKMYAVLPCGGIGVDSDTVWNEMHSS

SAVRMAVGCLLELAFKVAAGELKNGFAIIRPPGHHAEESTAMGFCFFNSVAITAKLLQ

QKLNVGKVLIVDWDIHHGNGTQQAFYNDPSVLYISLHRYDNGNFFPGSGAPEEVGGGP

GVGYNVNVAWTGGVDPPIGDVEYLTAFRTVVMPIAHEFSPDVVTLVSAGFDAVEGHLSP

**LGGYSVTARCFGHLTRQLMTLAGGRVVLALEGGHDLTAICDASEACVSALLSVELQPL** 

**DELVLQQKPNINAVATLEKVIETQSKHWSCVQKFAAGLGRSLREAQAGETEEAETVSA** 

MALLSVGAEQAQAAAAREHSPRPAEEPMEQEPAL (SEQ ID NO:9)

the fight of H 15 Hold flow the the thing the H

H H H H 26 offen 4 H T

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FIG.5B-1

FIG. 5B

cagagtccc tccctgctgc gtgccactcc acggtaggca aagcagaagc aggcagccca ttgctggggg caggaagacc caggttaagg ggtgctggat caggcgccc cctgctgccc acaggtgtgg gtgcaccctg attcctggct cgggcatgcc ccagtcctcc cctcttcacc cacatcctct accgctgccg gcaggaggtc tgagagcaca ggattgcatc ggaggagcct gcaggtgtac gaacacacac cagcatgcgg gttcctggag ggagctgccc cctcattgct agttcatgag ggagccccca ccgtcaagca gcatgtgcgg agcagagcac gtgtggccac ctcagtcctc agcaccagca tgggccgtac tgacggagca ccacagagag aggaggagga tgcagccttt ccaagacagg ggcccgactt ctgaccggca cgggagggct caccaggccc ccagaccagc gaggcgacg caggcccggc acgggtgaac ctgagccgca atgcaacaac aagatcctca gaggaggagc gaggatgggg gctgaggagg gccagccgc aagcaccagt gggtggcacg gaagagccc gttcatgcta cgtggcactg gttgctggag cccactagtg gcatcggccc gcagctggtc acagctgggc tgaggagaca gaccatgccc ggacgaggaa cgagagtggt gttctcagat cactgtgccc ccctgcggca gcctgctggg agcatgtgct acgggcagtc agctcccgcg aggccctgca agcagcagct ccaccacc agggagccct tggaggagga acgaggaggg acaaaaact tcagcctggc ctgggggcat tctacgacac 301 361 421 481 541 601 661

FIG. 5B-1

ppnorffi

FIG

tgcttcttca acagtggtga gcagtggcca ctgcttagca gtgcactctg gacagcaaga ggatttgcca aaggtcctca aatgacccct ggctctgggg gcatggacag tttgatgctg tttggccact gaggaggcc aagttcgccg gccgagactg tgacgccccg taaaaacaaa ggcatcgggg atggcagtgg ctcagtgtag gcagcccggg ggagacaggc gatccagaca cttcttcca agcetteagg ctccgccggg cgccagatgt gcctgccctg ttttttctat gcagaagcta cacgggattc gaacgtgggc ggcgttctat tgtgaacgtg gctggccctg ctcggctctg caacatcaac gccttgtggg gctcaagaat ctgtgtgcag ggccgaggag tgctgtgcgt ccaggctgcg cccggctgca tggggtacaa cgctagatga agtaccttac tggtcctagt tggagcagga attttgttta ccctcaaccg atgctgtgct actcctccag ctgcaggaga aatccacagc agcagaagtt gcacccagca acaacgggaa actctgtcac gccgggtggt agcaaaagcc aacactggag aagcaggtga ccgagcaggc aggettgtgt agcatctggt tcacctgatg cgcaaagcca gggaccagtc ggagacgtgg ctgggtggct gaggagccca caccattgtg cagaagatgt aatgagatgc ggaccaggcg ctggcagggg gatgcctctg gcagtcttgc atccagagca cgagaggccc tcggtggggg ttcaaggtgg cacgccgagg aaactcctac catggcaatg catcgctatg ttc (SEQ ID NO:10) ccggatccag tctgtctcct caggccggca ctctcggctt gatccgaggt cctgctctac ggagctggcc ggttggtgga ccacgagttc gctgatgacc cgccatctgt cttggatgag ccggtccctg ggccttgctg cccatcagc caccottotog cccaggacac catcaccgca ggacattcac ccccccatt agtcatcgag catctctctg agcatgctgg ttgaaggaca agtgcgagcg aataccacac tgcccattgc tgaccaggca agttgctcgg tggacagtga atgacttgac agctgcagcc gacacata aagtcacaca ctgtgctcta ctcctgaaga gaggtgtgga gctgcctgct tcatccggcc actctgtagc tcgtggactg cgctagagaa ctggtctggg tgagcgccat aacacagccc 1621 1681 1741 1081 1141 1201 1261 1321 1381 1441 1501 1561 1801 1861 1921 1981 2041 2101 2161

# FIG. 5B-2

IJ

42P. 37

RAFTSMA:

FIG.

SUBCLASS

FIG. 6A

| FIG. 68-1<br>FIG. 68-3<br>FIG. 68-3 |  |  | G. | FIG. 6B |
|-------------------------------------|--|--|----|---------|
|-------------------------------------|--|--|----|---------|

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| ggcggagtgg | ggattccacc | ctccagtgtc | tctagcggag | cctaatcgtg | tggcttggtg | ggaaggccct | tagatgagtg |     |
|------------|------------|------------|------------|------------|------------|------------|------------|-----|
| ggcgggatct | caaccggcca | ccctcagga  | ctatccccaa | tggaagaaga | tggctggcac | acagcttccc | gcctcctaga |     |
| aaacgctagg | actatgacct | ccccagtcgc | gttccccgct | ggccaagcaa | gctgaagcac | ctctgggatg | atccaggagg |     |
| gggctggttg | agcctcctca | taggcagaac | aaagggagcc | gaagaagctc | gaacctcgag | attccattgc | ggagcaactg | •   |
| ctgaggagcg | gcaggggcca | agcgaagaag | gaaatattaa | aaggcaaaat | ggatggatct | agttaaatga | atgccatcaa |     |
| gggcagtccc | aagaaccgcg | acaaccaggc | acttcgaagc | gtaaagaaga | ggactgcaag | ttggatgagc | gagcggctcc | A A |
| Н          | <b>61</b>  | 121        | 181        | 241        | 301        | 361        | 421        | 7   |

FIG. 6B-

| ( |             | J      |
|---|-------------|--------|
| ב | Y           | ,<br>נ |
|   | ,<br>,<br>, |        |
| Ī | L           | _      |

| ggatccgctg | ctgcacgggg | ggctttgatg | ggtctcagct | aactggtgct | tttaacccag | 2281     |
|------------|------------|------------|------------|------------|------------|----------|
| tgcctacgag | tgcttcccat | catcgcctgg | agctgcctgg | ctgactacct | tgggt      | 22       |
| cgggccccgc | tggcatggaa | accgtcaacg | cacaggette | gcc        | gatcgg     | H        |
| tgccagcagc | gggatgaggg | ttccccatgg | tggcaccttc | gctatgatca | tccctgcacc | $\vdash$ |
| gctatatgtg | accccagtgt | tttgaggatg | tcagcacatg | aatg       | บ          | 4        |
| ggattgggat | tcctgattgt | ບ          | cagtgggcat | บ          | gctcgccatg | 98       |
| ggctgtggct | tcaactctgt | tttigctttt | agcttgcggt | agcaggatgc | caccacgcag |          |
| tcccccagga | ctgtggtgcg | aatggtgctg | agaggtcctg | tgctctcagg | gtggaggctg | 98       |
| ctgccgcctg | ctggcgctgc | cagcttgcca | cgcctgtgca | ccagtacctt | tatatctgcc | 80       |
| tgactccatc | gttccaactt | caccgtgaga | ccgggagctg | aaatgaaaac | gccacagaga | 74       |
| tcatctccgg | agtacgtggg | cacagtgctg | gctcacctgt | aggctgagct | cctgccacag | 68       |
| gacaccgcgc | gcctcaccct | gaaggaaat  | gctgggcctt | gtctggagga | atcatgtgcc | 1621     |
| catcttgcgg | taccccagcg | caccctgagg | ggacagccac | gcaacttgtg | atgaatcact | 26       |
| ccaaaatatg | tggtctatga | cgcacagggc | gctacagtct | calggccagt | ccaatcctga | 50       |
| ccctgtgctc | cctgggagcc | gaggaaggac | ggagagcgag | acaatgtaga | atggaggagg | 44       |
| gagggacaac | agaccgtgga | agatcaactg | ggttcttgtg | ccttctggga | gcccttgagc | 38       |
| tgctctggaa | cagtttcctg | gcccaggctt | ctgccggagc | ctggtgcccc | ccggagtcac | 32       |
| ttgccccatg | tgggagaccc | cacaccette | tgattagata | aaggcgtcag | gccctggctg | 26       |
| caacctccgc | agggtggcta | ctgtctctgg | caagctgatc | tggcaggagg | ctcatgggtc | 20       |
| aacccacctg | tegeceaget | ccggcagggt | ggccgccact | agggcgagat | ggggacccca | 14       |
| tgccctgcaa | ctggatttga | ctggtggccg | tcagctggtc | agctccagcc | gtcgccctcg | 08       |
| cctgctgcca | tcctgcacgt | attgctgctt | tgctgactac | ggatgcggga | aaccaggtgg | 02       |
| tgtgccttgg | ataccatcaa | ggccaaggat | tttcggccaa | ccaccacagg | tctaactggt | 9        |
| cctgaaggcc | tctggcccca | cagggtaggt | ccgctacgag | tctccatcca | gtcctctatt | 0        |
| ggaccccagt | ccttcgacca | acacagttca | cggtcaagga | atgtgcacca | gtagattggg |          |
| ggtccttatc | gcacccggag | cagaaacacc | ctatgctcaa | tggcagcccg | cacgtggctg | $\infty$ |
| catgttcaac | atggctattg | agtcttatgg | cgcccagcac | ctggacatca | attaggcctc | 2        |
| catggccatc | tccggaacgg | ggggctgaga | tgaggtaatg | ggctggtgga | tctgtcctca |          |
| ggcctcaggc | gtgcctgcct | tcatactcct | gcatccgaac | cagtttatct | acccacgact |          |
| cctagcagac | aactccgtgt | aatgaggag  | ccagtacatg | tggaaacaac | attgacctga |          |

ccacctgct

tgagggttat

aggtgtcacc

ggggctgcc

2341

1. 0 8 8 15 mm 11 mm 12 mm 12

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FIG. 6B-3 gttgcatatg ggagccgata gccccaagag gcatggcaag cagctcagtg taactggcag gaaagggggg ggagggagt caagctgtt (SEQ ID NO: agcccagaag aacattggcg taataaagta ccactactcc tcatgaggat

catctcagag gaccctgcca ccatcgcaga cagttctaag gatgaccaca atttggggaa aggagctaca gactacgtca cacagaccac tgtgacacca aaattctgga tgaggcccac ctcccactgc gatgggcctt tcaggaccag ggcagccatt cactccggac ctcagaggat cagtacactg agaatctcag ggctgattcg cctagacgtg ctcttgctat tcaggcctat gtttggggag ttgaggggca ttaatacttt acctgacatc ccatccaagt aaggaccctc cctcggcatc tggccctcac ccatttctga tcgggggagc accagaccac cactggacca tattttatgc cttcaccttc gagggtagc catcgcccgc cacccttgct tagctgagcg aggctgtagg tagcctcgag agatatctcc agggggcctc gtcaggacat ctgcagcagg gggtgtgtct aacaccatgg gttactactg accagaacaa tatttaagtg gccacctca ggagacccac tcagcctggc aacatcgccc tacacatga ggtggctata atcactgaga ctggcccaga gccattctgg gagggagcca caaactcctc actacaccc agcgaacctC gatcaggcca tgccccatac caagagaact cacatgctcc tacggtccct gaagacagag aaacctaggt gggaaagtca acagctgtgg gaggaggctg acctcagagg gcagctggag taccttggat caagagtgct ttccaggctg tatcctagag gaccacctca tgtgcaggga ggagctaggc ggtggcagta tggaacaatc catcaatggc catcgacctg agccccagaa tgcaactccc attgtggatc atacatactt cctggcctca catgaaggca ccaaccagcc agcaggcatg taactcagag gggagccact tgtgggagga gggccagact ggcagccatg cgagctgatc accaggagag gggcctcact agatgtgaag gcgacgatta tcctcagcca ttccagcctg tatcaggggc ccatctcgga gtggtcgtta acccacacta gaatatcctt gcattatcct cctgcactcg gcttacgggt agaaggcacc aggttctgga caggccagac cagccacagg tgctgggcca cagaggagac gagccacgct cagggggcac caacctcacc tcaggacctt aggagaacct agggatctag gtccccattc gtgggactg aggetetect gccagtggcc tccatggctg cggcccccac tactggcgca ttggtcacca cgagaaaga gagtccactc ccctcagagg ggggagcca cagaccacct gctgttgggg ctggcccaga gaggaggctc cagaccccc attgggagtc gccccaggag atgctgacgc ctgccctggt acccaacctt caggtctacc cacccgctgg gtccaccacc gatatgcccc gatagaccag atcccatcct taagagaact 3901 3961 4021 4081 2401 2461 2521 2581 2641 2701 2761 2821 2881 2941 3001 3061 3121 3181 3241 3301 3361 3421 3481 3541 3601 3661 3721 3781 3841

kasieelgsv elhssnaarw qlqqqskask gagsgegfnv aplggyhvsa seegwkqkpq dtpmpelgvg gipyrtlepi rrknpllrkehptlgprgpi tpart1pf1t weqqrlagrl pfhfagsimt sakpsekprl rsvepmrlsm lertvhpnsp sqarvlssse agfdaaeghp lrykpkksle pilgdsdrrt lkthvqvikr rsqceclrgr vgvdtdtiwn ffnsvajacr fpgsgavdev 11tvpg1gp1 plaahpavii allgnrvdpl spndsehgpn 11dpsgshap evilkkqqaa rktvsepnlk adhstamgfc hlflaglqqq pgpmqprleq hgqpeargpa pasisapepa iwsrlqergl rmfemlpcgg slhrhddgnf efspdlvlvs icdaseacva algrpgrlhh assvvkgkla **lppsatappp** ssstpasgcs ddglehrelg lsraqsspaa hpehagrigs ngklagiiag favvrppghh frivvmpiar alegghdlta psdppehfpl clpsrlqpil fyqdpsvlyi ID NO:13 aetlgdssps Wplsrtrsep tdggggggvv lplaqgghrp tnplsr1k1d kvasrelkng pmgdpeylaa dpgaq (SEQ vepppept11 hkdkskrsav ssflppvpsi phglepeagg hqcscgdnsr vhhgngtqqt mnlaggavvl gliydsvmlk mdlrvgqrpp sappslrrrp lgsphtplfl terlsgsglh rqipsaedle prgstgdcvi hserhv11yg aagsvtdlaf askilivdwd nvawaggldp kcfgymtggl etegatrsml pachplaggr pqeqelrqll 181 241 301 361 421 481 541 601 661 721

## FIG. 7/

| FIG. 7B-1 | FIG. 7B-2 |
|-----------|-----------|
|           |           |

| <b>T</b> | ataataccta | ccttgcagga | ccacgacagg       | attaagtgag | gaaaaaccc  | catgagagtg   |
|----------|------------|------------|------------------|------------|------------|--------------|
|          | ttttgccatt | gtcaagtgag | cctgagggag       | gctgaggggg | gatcaggctg | tatcatgccc   |
| 2        | ccgaggacaa | actttccagt | ttaccctgct       | acctatatat | gtccctaggc | tgccccaggc   |
| $\infty$ | cctgcgcaga | cacaccaggc | cctcagccgc       | agcccatgga | cctgcgggtg | ggccagcggc   |
| 4        | ccccagtgga | gacacaca   | gagcccacat       | tgctggccct | gcagcgtccc | cagcgcctgc   |
| 301      | accaccacct | cttcctagca | ggcctgcagc       | agcagcgctc | ggtggagccc | atgaggctct   |
| 9        | ccatggacac | gccgacgccc | gagttgcagg       | tgggacccca | ggaacaagag | ctgcggcagc   |
| 2        | ttctccacaa | ggacaagagc | aagcgaagtg       | ctgtagccag | cagcgtggtc | aagcagaagc   |
| Φ        | tagcggaggt | gattctgaaa | aaacagcagg       | cggccctaga | aagaacagtc | catcccaaca   |
| 4        | gccccggcat | tccctacaga | acccggagc        | ccctggagac | ggaaggagcc | acccgctcca   |
| 0        | tgctcagcag | ccttccgcct | cctgctccca       | gcccgcccag | tgacccccca | gagcactccc   |
| 661      | ctctgcgcaa | gacagtctct | gagcccaacc       | tgaagctgcg | ccataagccc | aagaagtccc   |
| 0        | cggagcggag | gaagaatcca | ctgctccgaa       | aggagagtgc | gcccccagc  | ೦೮೮೦ರಿಥೆ೦೦೦೦ |
| 781      | ggcccgcaga | gaccctcgga | gactcctccc       | caagtagtag | cagcacgccc | gcatcagggt   |
| 4        | gcagtccccc | caatgacagc | gagcacggcc       | ccaatcccat | cctgggcgac | agtgaccgca   |
| 0        | ggacccatcc | gactctgggc | ငငငငရွစ္စရွစ္တင္ | caatcctggg | gagcccccac | acteceetet   |
| 9        | tcctgcccca | tggcttggag | cccgaggctg       | ggggcacctt | gaaataaga  | ctgcagccca   |
| 02       | ttactatact | ggacccctca | ggctctcatg       | ccccgctgct | gactgtgccc | gggcttgggc   |
| 08       | ccttgccctt | ccactttgcc | cagtccttaa       | tgaccaccga | gagatatat  | gggtcaggcc   |
| 1141     | tccactggcc | actgagccgg | actcgctcag       | agcccctgcc | ccccagtgcc | accgctcccc   |
|          | caccdccddd | ccccatgcag | ccccgcctgg       | agcagctcaa | aactcacgtc | caggtgatca   |
| 26       | agaggtcagc | caagccgagt | gagaagccc        | ggctgcggca | gataccctcg | gctgaagacc   |
| 1321     | tggagacaga | tggcggggga | ccgggccagg       | tggtggacga | cggcccggag | cacagggagc   |

ggaggtctgg atgacgcagc ctctctggag cctcaggtgt gggacactg tcttccccag teggtcatge ggccgcatcc tgtctccgag gtgctcctct gggctcctgg gacaccatct actgacctcg ccccaggac gccatcgcct attgtagact agtgtgctct gctgtggatg acgcccatcg gctgagggtc catgacctca agggtggatc ctcctgtcca agtgaccgca gctggtggag catgcccttg ctctccagct tagagatcct cccagggagc ggagggtggc agegeetgge cctgggtctt tgacagttat gggcagcacc gatctatgac ccagtgtgag tgagcggcac tggcagtgtc tgtggtgcgg caagatcctc ccaagaccc gggagtggg ggcctgggct gatagtcgtg atttgatgct ttttggatac tctgggtaac atgccactcg aagtggaggc cctcggagca gcccgcccac ccagcagcac ggcccgagtc ggagcacgcc gaagctggca caactcagtg ccgggctcag ggtggacact tgctggcctt tggctgctct cccaacctca ggctgcatgc gacaaagaag gaagataggc ggaaccatct agcccccatt ctgcctgctt atggtttcgc tctgcttctt gcaaggccag aaaccttcta acttcttccc atgtcaatgt ctgctttcag tgtctgccgg ctgccaaatg aagataatat aggtacacta gctgggccgc ggctccccg gcaggcaccc tggacaacgg gtggggttgg ggcctctgtc ctgccagcca ccacagggct ggcctcggag gagctaaaga gccatgggct ggcacccagc gacgacggca gagggcttca taccatgttt ggcgcagtgg gaggcctgtg aaacagaaac taaatactgg gccaggggct ccctggcaat agagaacagc ctggctgggc cgcctcaaac aatgcagccc agcaaggcca gagtacctgg ctagtcctgg catcctggct ctaaggctct gccagaggcc gccccagagc ctgcccttca ggtgacaaca ctgccctgtg ggtgggcacc caggagcggg gagctgcagt C (SEQ ID NO:14 ctcttctaac agttggaacc ctatgaatct cctggcagga gggtgcacag tgcctagagt tctctgtggg ctctccagac acLgggtggc tgacgcctct agaaggctgg gcagcccgag acagcagcga tgccaggacc gtgctcctgc gtcccggctg ctccctggaa cccgctcagc gtttgagatg tcattccLcc ggcttctcgt tcattcaaca gcaacagcag ccatggcaac gcatcgccat tggcagcggt gggggatcct tctggcccag ctcactgtca cccttcaga gaggaagaac ggacctggtt gtgggcaagt accegecee aactgatgaa cagccatctg gccgtgatcc ctggcgtccc accatgcaga aggtagggc gactcctggg gtgagaaat ccgcacctgc cagagaccc tgaagcacca gccggaaggc acggcaccaa cacagcggat ggaatgagct ccttcaaagt gccggcagct gggacgtgca acatctccct accccccat cccgagagtt tgggccatgg tgctctggga tgctgcttcc agagcatctg 3001 3061 3121 2881 2941 2461 2521 2641 2701 2761 2821 1441 1981 2041 2101 2161 2221 2281 2341 2401 2581 1501 1561 1621 1681 1741 1801 1861 1921

scrpdrneph hkqmrivkpk rilyvdld1h ilqwqlatli yaaaiggati iqdgiqdeky dcpategifd pvgigkclky lakipkrasm vhslieayal gilrlrrkfe kgryysvnvp gpdyvleitp htdaylqhlq kvsqegdddh pdsieyglgy gfcylndavl tgdvsdvglg gdpmcsfnmt *ipdbefftay* vyqafnpkav vlqlgadtia tarcwtyltg vilgktlsse gnlkhvv (SEQ ID NO:15) gqslvpvyiy speyvsmcds ftskvmtvsl hkfspgffpg ckvainwsgg whhakkdeas yqicesvlke lggggynlan meepeepads vasmeematf taaqclidgm riqqilnyik hgdgvedafs 181 241 301 361 61 121

FIG. 8A

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|              |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            | 8<br>B      |
|--------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|-------------|
| grandatera   | totataqtoo | gtatggtgca | ctaaagtggc | tccagaaggt | gttatgactg | cgatcacagc | gagggtggca | tcctgggaat | tgcaccatgg | ccctgcacaa | tagggaaggg | aatattacca | cagtggtctt | tgactccagt | tcatttcggg | ccggggtcat | catatggtcc | cccaccgaat | tgacagaaag | tttatgcaag | tgaaaatttc | ccagagtcct | taaaaaaaca | tggggagggg | tcaccagttt | ngtggagccc | Ē           |
| gattttaagg   | ccggtttata | aaacgggcca | atagttaagc | ctgcagcatc | tatgggctag | ggaggggcta | aactggtctg | aatgatgctg | gattcggatc | atgaccgtgt | gacgttggcc | caagatgaaa | aatcccaaag | tcctttaaca | ttggcaacac | acatacttga | ttttcacag  | cgcaatgagc | gtggtctagt | agacagcgtg | aattacttcc | ggcaggcacc | agttcttatt | ttaagcgaat | atgagagcag | ggaccancca | ID NO:16)   |
| מנשנימשמששני | gtcgctggtc | caagatccc  | gcaaatgagg | tgatgcttat | ctccatagaa | agcagctata | agtagcaatc | tegttatete | tccctacgtg | ctccaaagtc | tgacgtgtcc | ggatggcata | ccaagccttt | tcccatgtgc | tcaatggcag | tcgatgctgg | agatcatgag | ccggccagac | tctgaagcat | cctataatga | atttgaaaga | ggggtgaaga | ccacatttaa | aaaattattt | cagaagctgg | tngggcctcn | gagg (SEQ : |
| gagaattaa    | acagtgggca | actccctggc | cactgcataa | ccttccacac | atcatccgga | ttgactatgc | gaatgtgcaa | catctggttt | ttgagcgtat | tcagtttcac | caggaacagg | tgcccatcca | aggaagtata | tagctgggga | agtacatccc | ccaacacggc | ctgagatccc | cgccaagctg | tcaaagggaa | aggagtggtg | tgcagggaaa | ctggcttcct | aggagatarc | ttaatctttg | tgaaacagat | caggcagggn | ngcagactgg  |
| acquacticat  | aaccg      | tatg       | gaagcatatg | gagatggcca | ggcgatgatg | gaagggatat | ctgattgacg | aaagatgaag | cgacggaaat | gaagacgcat | ggatttttcc | agtgtaaatg | agtgtactaa | gccgacacaa | aagtgtctca | tataaccttg | acactatcct | ctggaaatca | ctcaactaca | tccagagctg | aatttgtgac | caagtggcag | taggggaaga | aatgaaattt | tcatcttaaa | aggcagctga | ggtactgatc  |
| gaaattegge   | ggagccggag | agtatgt    | ttctttgatt | ctccatggag | cagccaagag | cccagccact | tgcccaatgc | tcatgcaaag | attacgattg | agatggtgta | attctcccca | acggtactac | gatctgcgaa | acagctggga | gggaattggc | aggaggaggc | cctagggaaa | tgattatgtg | ccaacaaatc | agatcaggtt | cagtttgrgg | caaggggcat | caactggacc | cacacacaca | agtattttaa | gtagggcagg | tgggagagan  |
| •            | 61         |            | $\infty$   | 241        | 0          | 9          |            | 481        |            | 0          | 9          | 3          | $\infty$   | 4          | 901        | 961        | 02         | 1081       | 4          | 0          |            | 2          | 1381       | 1441       | 1501       | 9          | 1621        |

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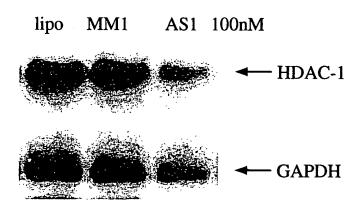


FIG. 9A

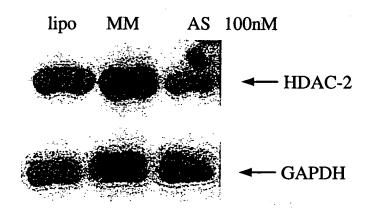


FIG. 9B

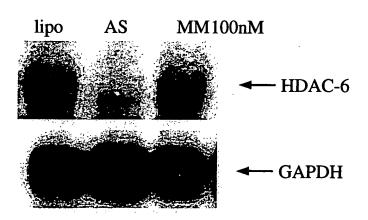


FIG. 9C

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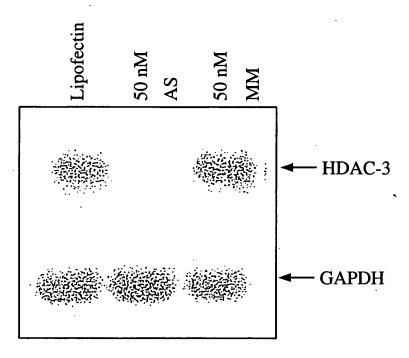


FIG. 9D

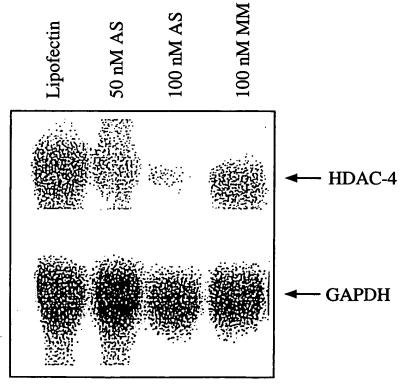


FIG OF

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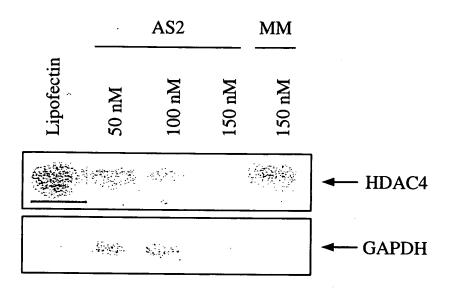
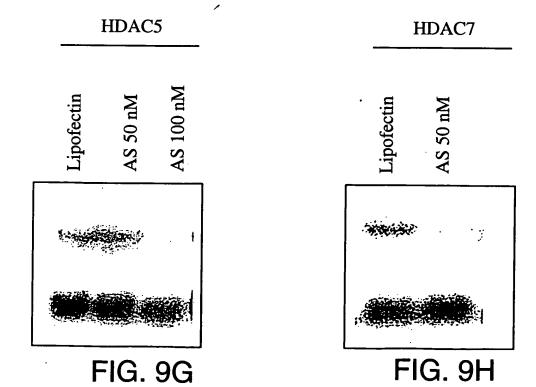
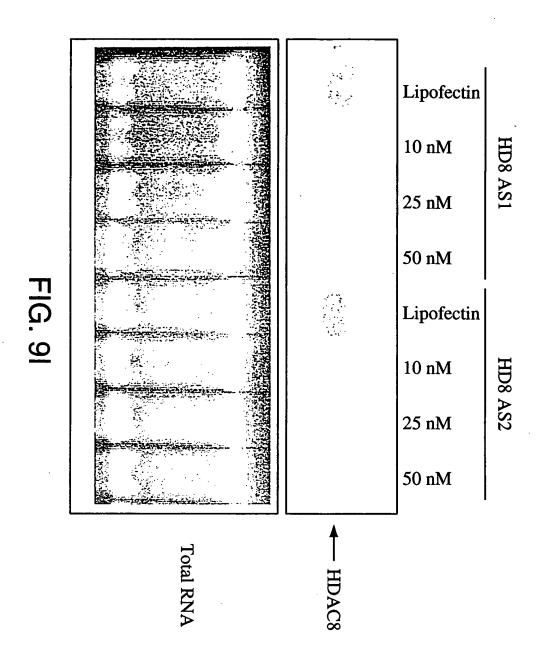
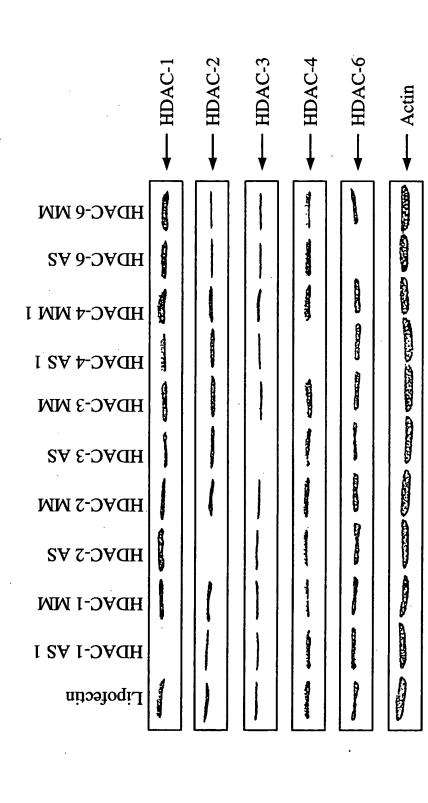


FIG. 9F







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Oligonucleotide cone – 50nM

NS = Non-specific control

3 day treatment

MM = Mismatch AS = Antisense

FIG. 10A

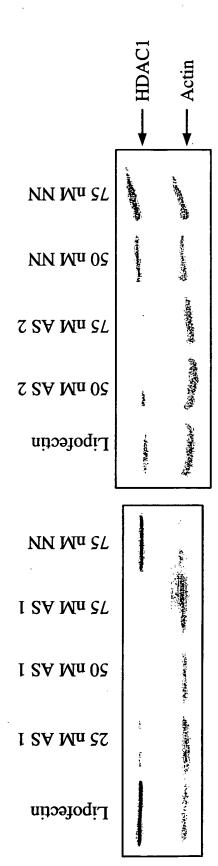
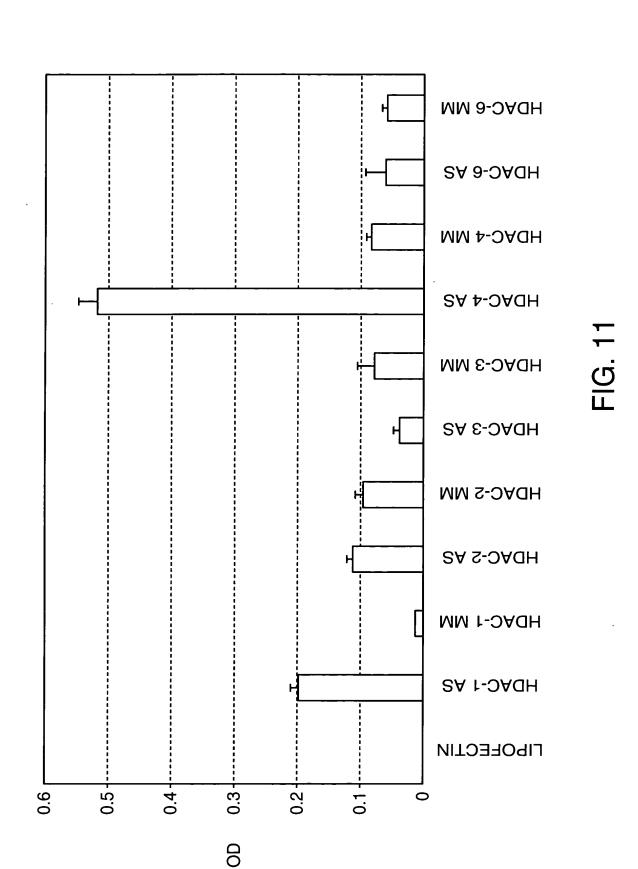


FIG. 10B

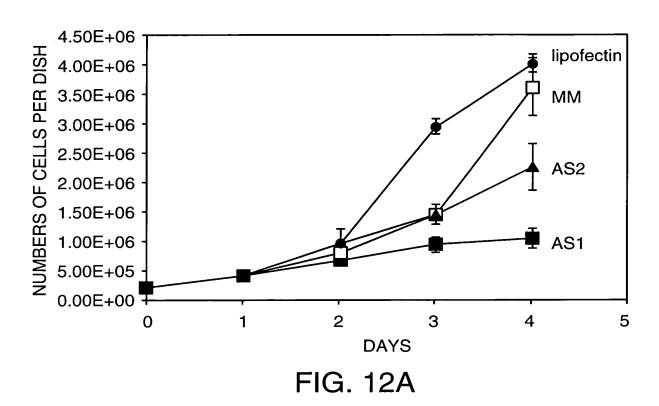
ET FIG.

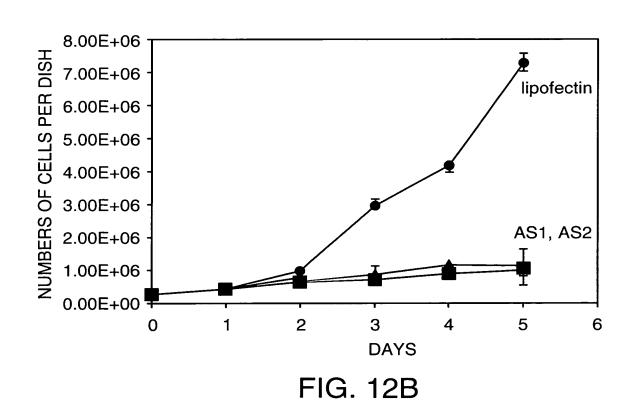
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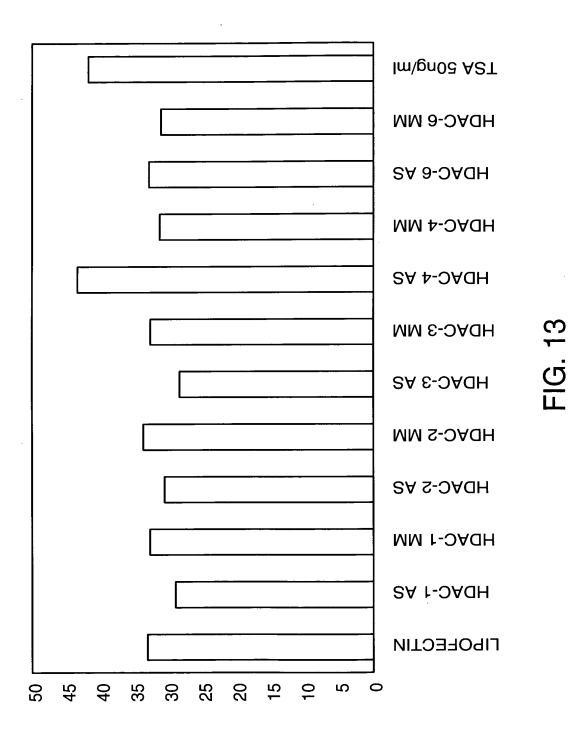


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% OF CELLS WITH DNA CONTENT (>=2N)

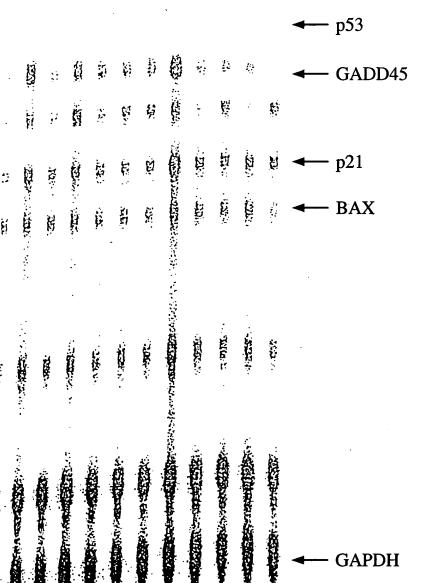


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**GAPDH** 

FIG. 14

- Complete C HAN THE WASHINGTON OF THE PARTY OF THE PARTY

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|        |        | ← p21             | ← Actin                                 |
|--------|--------|-------------------|---|
|        | AST    |                   |   |
| HDAC-6 | MM     |                   |   |
| HD/    | SA     |                   | *************************************** |
| C-4    | MM     |                   |   |
| HDAC-4 | SA     |                   | A CASA                                  |
| C-3    | MM     | CENTRAL PROPERTY. |   |
| HDAC-3 | SA     |                   | * Transcient                            |
| C-7    | MM     | O AR              |   |
| HDAC-2 | SA     | 4                 |   |
| C-1    | MM     | 0                 |   |
| HDAC-1 | SA     | G. C.             |   |
| ctin   | oloqiJ | - Carrier St.     |   |

FIG. 15

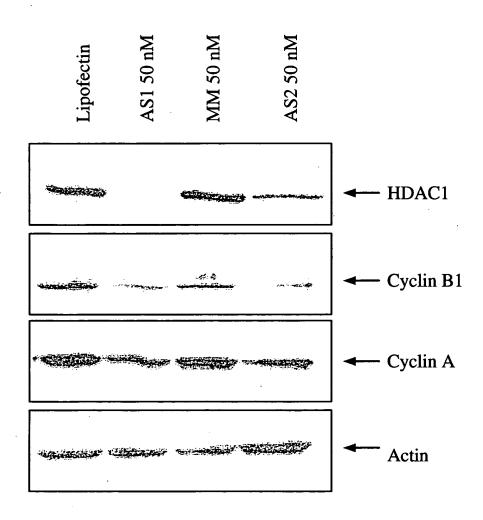
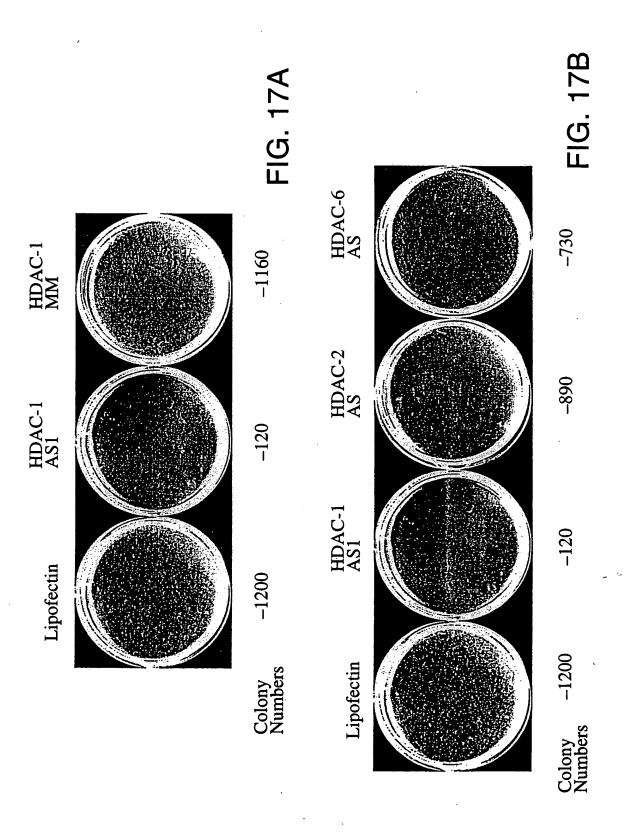


FIG. 16



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## Compound 3

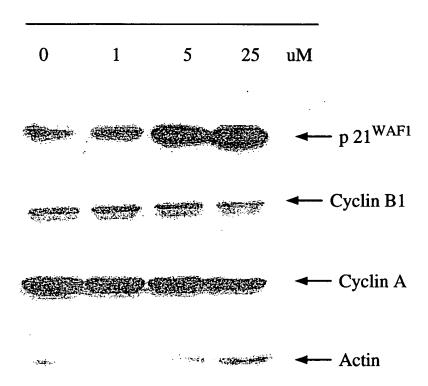


FIG. 18